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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,579	10/16/2003	James C. Chen	59785-8	7765

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EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/687,579	CHEN, JAMES C.	
	Examiner	Art Unit	
	Charleswort Rae	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *22-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 06/16/06, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Status of the Claims

Claims 1-24 are pending in this application and are the subject of the Office action. Claims 22-24 have been withdrawn from consideration for purposes of examination for being directed towards non-elected subject matter and (37 CFR 1.142(b))

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention

Claim rejections – 112 – First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling as any person skilled in the art would not be enabled

based on the written specification to make and use the instant invention without carrying out undue experimentation. For example, a critical or essential step recited in claim 1, "wherein said PDT drug is cleared from the skin and subcutaneous tissues of the subject prior to said irradiation," for practicing the invention as claimed, is not enabled to achieve the claimed utility of the method for photodynamic therapy i.e. reduction of adipose tissue or adipocytes. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Applicant's argument that this rejection is overcome by the amendment of claims 1 and 8 is not deemed persuasive for the reasons set forth below because someone of skill in the art would not be able to make and use the instant invention as claimed. In particular, claim 1 recites the critical or essential step "wherein said PDT drug is cleared from the skin and subcutaneous tissues of the subject prior to irradiation." The specification does not provide a concise definition to the term "cleared from the skin and subcutaneous tissues" as recited in claim 1. One meaning ascribed to the word "clear" is "all the way" (The Merriam-Webster New Collegiate Dictionary (1981), pg 205). The limitation "cleared from the skin and subcutaneous tissues" is construed to mean "absolutely removed" or "completely cleared" from the skin and subcutaneous tissues." To the extent that the photosensitizing agent must be cleared completely from the skin and subcutaneous tissue prior to irradiation, someone of skill in the art would not be able to make and use the instant invention as claimed.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if its is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth in *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman* 230 USPQ 546 (BdApls 1986) at 547 the court cited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice that instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to a method for photodynamic therapy for the reduction of adipose tissue or adipocytes in a mammalian subject comprising: administering to the subject a therapeutically effective amount of a photosensitizing agent or a photosensitizing agent delivery system, wherein said photosensitizing agent or said photosensitizing agent delivery system selectively localizes in the adipose tissue or the adipocytes; irradiating at least a portion of the subject with light at a wavelength absorbed by said photosensitizing agent, wherein said light is provided by a light source; and wherein said irradiation is administered at a relatively low fluence rate that results in the activation of said photosensitizing agent; and wherein said PDT drug is cleared from the skin and subcutaneous tissues of the subject prior to said irradiation. Applicant assert's that there is a long-felt need to a method to treat obesity by reducing adipose tissue which method is noninvasive or minimally invasive and results in homogenous adipose tissue reduction (page 2, lines 4-6).

With respect to the prior art, Nelson et al. disclose that there are unanswered questions regarding Npe6 with respect to delineation of light and drug dosimetry parameters and possible uptake in other organs such as liver, intestine, spleen, and kidney (Nelson et al. In vivo studies on the utilization of mono-l-aspartyl chlorine

(Npe6) for photodynamic therapy. Cancer Research 47, pgs. 4681-4685, September, 1987). The uptake of the photosensitizing agent by non-target tissues would affect the distribution of the photosensitizing agent, which would reasonably affect the reliability/predictability of the localization of the photosensitizing agent in the target cells/tissue (specification, page 11, lines 3-8). To the extent that fat cell deposits are found in the subcutaneous and the abdominal tissues, coupled with the fact that upper body fat seems to be functionally different from lower body fat, uptake of the photosensitizing agent by abdominal tissue would necessarily affect the clearance of the photosensitizing agent and its attendant toxic effects. (In:Cecil Textbook of Medicine (2000): column 1, lines 1-29; see also Dougherty et al. page 900, column 1, line 17 to column 2, line 1). Thus, irradiation of different portions of the subjects would reasonably lead to unpredictable results in the absence of evidence to the contrary.

Dougherty et al. (Dougherty et al. Photodynamic Therapy. J Natl Cancer inst 199; 90:889-905) teaches that photodynamic therapy involves administration of a tumor-localizing photosensitizing agent, followed by activation of the agent by light of a specific wavelength (abstract; see also instant Specification, page 8, lines 16-22). If the photosensitizing agent is completely cleared from the skin and subcutaneous tissues prior to irradiation, then it necessarily flows that administration of light to the skin and subcutaneous tissues would not result in photactivation of the photosensitizing agent and the intended result of the instant photodynamic method

would not be achieved. Also, Dougherty et al. also disclose that there is a relatively long learning curve in learning how to apply PDT (page 900, column 1, 15-16).

Robinson et al. (U.S. Patent 6,444,194) disclose that many of the correlation's found in one group of photosensitizing compounds do not transfer to different groups of photosensitizing compounds (column 2, lines 14-16). Robinson et al. further disclose that a different class of compound, that inherently has its own spatial and geometric parameters, must have its own structure-activity relationships investigated even though this in itself is a large time consuming process with ultimately no guarantees of enhanced localization or improved PDT efficacy (column 2, lines 14-24).

Thus, one skilled in the art would not be able to reasonably practice the instant method for photodynamic therapy for the reduction of adipose tissue or adipocytes in a mammalian subject based on the disclosed teachings of the instant application without undue experimentation.

The relative skill of those in the art is generally that of a Ph.D. or M.D. It is noted that the therapeutic and pharmaceutical arts are generally unpredictable, requiring each embodiment to be individually assessed for pharmaceutical and therapeutic efficacy, respectively. The more unpredictable an area, the more specific enablement is necessary in order to satisfy the statue. (see *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970)).

The breadth of the claims

The claims vary in breadth from very broad to narrow. For example, claim 1 is very broad and encompasses all photosensitizing agents, all photosensitizing agents

delivery systems, and prodrugs thereof, multiple different routes of aministration for the photosensitizing agents, and all mammalian species. The "irradiating at least a portion of the subject" limitation is also very broad. "At least a portion of the subject" is very broad and "irridation" as recited in claim 1 encompasses internal and external sources of irradiation. Claim 19 is narrower and is directed to local administration of the photosensitizing agent. Further, local administration of a photosensitizing agent to a small local area of skin would reasonably be expected to achieve different effects with respect to the localization and therapeutic effects of the photosensitizing agent on adipose tissue/adipocytes and the clearance of the photosensitizing agent as compared to systemic or total body local administration of the photosensitizing agent in a patient. The limitation "selectively localizes in the adipose tissue or the adipocytes" encompasses both subcutaneous fat deposits and abdominal fat deposits, which are functionally different. As discussed above, the limitation "cleared from the skin and subcutaneous tissues of the subject prior to said irradiation" recited in claim 1 given its broadest reasonable possible interpretation is construed to mean that no amount of the photosensitizing drug may be present in the skin and subcutaneous tissues prior to irradiation. The instant invention also encompasses different routes of administration of the photosensitizing agents, which would reasonably be expected to result in a wide variability in pharmacokinetics and photodynamic effects of the photosensitizing.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples, Examples 1 and 2, are limited to the administration of mono-L-aspartyl chlorine e6 (Npe6) for photodynamic therapy for the reduction of adipose tissue or adipocytes in a mammalian subject. No reasonable correlation between the multiple different photosensitizing agents encompassed by the instant invention and the effect to be achieved (i.e. reduction of adipose tissue or adipocytes) is disclosed to provide guidance to someone of skill in the art to practice the instant invention without extensive experimentation.

Applicant's argument that examples are not required and that the instant invention is presumed to be enabled is not found persuasive to overcome the instant rejection in view of the level of uncertainty and unpredictability of the art.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to how photosensitizing agents encompassed by the instant invention can predictably effect reduction of adipose tissue or adipocytes in mammalian subject. The level of experimentation needed to determine the prodrugs of Npe6 and the other photosensitizing agents encompassed by the instant invention would necessarily involve undue experimentation.

Claim rejections – 35 USC 112 – Second Paragraph

The following is a quotation of the second paragraph of 35 USC 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the term "PDT," but fails to state the full meaning of the term at the first occurrence the term is recited in the claim. This limitation is vague and indefinite because it is not clear what "PDT" means. It is suggested that this specific rejection may be overcome by either replacing the term "PDT" with the full name or, alternatively, amend the claim by inserting the full name in parenthesis at the first occurrence of the term "PDT" in the claim.

Dependent claims 2-21 are rejected for the same under 35 U.S.C. 112, second paragraph as they fail to correct the deficiency of claim 1 from which they depend.

Claim 2 recites the term "selected from the group consisting of one or a plurality of:" 1) laser diodes; 2) light emitting diodes; 3) electroluminescent light sources; 4) incandescent light sources; 5) cold cathode fluorescent light sources; 6) organic polymer light sources; 7) or inorganic sources. Each member of the group (i.e. items 1-7) to which claim 2 is directed is presented in the plural form. This limitation is indefinite because it is not clear what the term "one or a plurality of" means.

Dependent claims 4, 5, 6, and 7 are rejected for the same reason under 35 U.S.C. 112, second paragraph as they fail to correct the deficiency of claim 2 from which they depend.

Claim 4 recites the term "said laser diode." However, claim 2 from which claim 4 depends recites the term "laser diodes." This limitation is indefinite because it lacks adequate antecedent basis.

Dependent claims 6 and 7 are rejected for the same reason under 112, second paragraph as they fail to correct the deficiency of claim 4 from which they depend.

Claim 7 recites the term "said light source is a mat?" This limitation is indefinite because it lacks adequate antecedent basis as this embodiment is not disclosed in claim 6, from which claim 7 depends.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 8 a.m. to 4:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like

assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

31 January 2007
CER

Ardin H. Marschel 2/5/07
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SUPERVISORY PATENT EXAMINER